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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,307	VAN DE WINKEL, JAN G.J.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20070102*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09,251,570; wich claims the benefit of the filing date of provisional application 60/074,967.

Claims 1-20 are currently pending and are the subject of examination in the present Office Action.

In view of applicant's amendment filed January 2, 2007, only the following ground of rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-10, 12, 13, and 15-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,635,600 to Fanger et al. (A4 on form PTO-1449) in view of U.S. Patent No. 5,922,845 to Deo et al (A on form PTO-892), both of record.

It was previously stated: "The claims are drawn to selectively reducing the number or actyivity of macrophages by administering a compound comprising a first agent that binds to the Fc receptor on a macrophage and a second agent that kills or reduces the activity of the macrophage. The claims further recite that the first agent does not bind to the same site as that bound by endogenous immunoglobulin. This recitation is being interpreted here as meaning that the first agent does not bind to the region of the Fc receptor that is responsible for binding to the Fc domain of an immunoglobulin.

The '600 patent teaches the use of a compound comprising a first agent that is an anti-Fc.gamma.R antibody (see entire disclosure, Abstract in particular) and a second agent that is a toxin, such as ricin (column 7, lines 3-10 in particular). The '600 patent teaches that the first agent can be a monoclonal antibody selected a group comprising mAbs 22, 32 and 197 (column 5, lines 12-16 in particular). The '600 patent teaches that the anti-FcR antibodies do not interfere with the binding of IgG to the Fc receptor (column 2, lines 15-24 in particular). The '600 patent teaches that this compound can be used to reduce the number of Fc receptors on the surface of a macrophage, thereby reducing the ability of the macrophage to clear antibody-coated self cells in a subject with rheumatoid arthritis (column 7, lines 32-40 in particular). The '600 patent teaches that the second agent can be a liposome containing anticancer drugs to kill macrophages in some hematological cancers (column 6, lines 58-65 in particular).

The '600 patent does not teach topical, subcutaneous or intradermal administration.

The '845 patent teaches that antibodies that bind to Fc receptors on macrophages can be administered subcutaneously (column 16, lines 14-33 in particular) or intradermally (column 21, lines 35-43 in particular).

The '600 patent does not teach first agent that is directed to Fc.alpha. receptors [claim 7].

The '845 patent teaches that macrophages can also be modulated using antibodies directed to Fc.alpha. receptors and that these anti- Fc.alpha. receptor antibodies do not interfere with Fc-mediated binding of endogenous IgA (see entire disclosure, column 1, lines 46-51 in particular). the '845 patent additionally teaches that the anti-FcR antibody can be a single chain antibody (column 2, lines 3-25 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the '600 and '845 patents. One would have been motivated to combine the teachings, with a reasonable expectation of success, because both teach the value of modulating the activity of macrophages for the treatment of certain conditions and by the teaching of the '845 patent that the compound can be applied locally via subcutaneous or intradermal means."

Applicant's arguments filed January 2, 2007 have been fully considered but they are not persuasive.

Applicant asserts that the references cannot be combined because the passage cited by the Examiner from the '600 patent allegedly teaches only the non-toxin-conjugated antibody's usage only against monocytic cells and the '845 patent teaches the use of the anti-Fc antibodies for enhancement, not killing.

This argument is not convincing because the passage from the '600 patent was particularly cited to highlight the '600 patents teaching regarding the killing of monocytes in rheumatoid arthritis. While the example cited in those particular lines does refer to "capping," the disclosure in the '600 patent also states that this is an exemplary use of the antibody of the invention. The preceding paragraph of the '600 patent also states that toxin-conjugated antibodies (of the same "antibodies of this invention") can be used for the killing/removal of any Fc bearing cell (column 7, lines 11-17 in particular). Again, killing of leukemic cells is exemplary, not limiting.

As far as the inclusion of the teachings of the '845 patent, the '845 patent is not required to show that the anti-Fc antibodies are used for reducing the number or activity of monocytes. The '845 patent was cited because it teaches the artisan that anti-Fc antibodies can be administered subcutaneously or intradermally and still be efficacious. The anti-Fc antibodies' of the '845 patent performed as expected, accordingly, this teaching would provide the artisan with a reasonable expectation of success that the anti-Fc antibodies of the '600 patent would perform their role as expected when administered via either of these routes.

2. The following NEW GROUND of rejection has been necessitated by applicant's amendment adding new claim 21.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claim 21 is drawn to the compound further comprising a "photosensitizing moiety." Applicant asserts that the photosensitizing moiety is supported throughout the specification as originally filed, especially at page 5, lines 10-13. However, page 5 , lines 5-13 are the only place in the specification that support can be found for this recitation. The passage does not describe any sort of function for the moiety, only that it would be "inactive when administered, but is activated by exposure to light." The specification does not describe what the activation of the moiety actually does. There is no description of any particular photosensitive agent or moiety found anywhere in the specification. Therefore, there is no description of what the moiety is, only that it can be attached and activated by light. There are no photosensitive moieties described that have any sort of function, such as having toxic properties, releasing a toxin from an antibody or crosslinking antibodies, for example. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,((CAFC, 1991) 18 USPQ2d 1016).

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115). See also, the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

4. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For reasons similar to those above, the specification is not enabling for practicing the claimed invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claim is drawn to a method using a compound comprising a photosensitizing moiety. As stated supra, the specification fails to disclose any particular properties or functions of a photosensitizing moiety. Furthermore, there does not appear to be even a single working example of an anti-Fc antibody compound comprising photosensitizing moiety having been made or used.

Based upon the paucity of guidance provided by the instant specification regarding the structure of the components of the fusion polypeptide, the lack of working examples and the inability to predict the function of the fusion construct based solely upon the binding properties on half of the complex, it would require an undue amount of experimentation on the part of one skilled in the art at the time the invention was made to make and use the claimed invention and this is not sanctioned by the statute.

5. The following also represent NEW GROUNDS of rejection. As these grounds of rejection were not necessitated by applicant's amendment, this rejection is made NON-FINAL.

Claim Objections

6. Claim 14 objected to because of the following informalities: the agent -- dichloromethylene diphosphonate—is misspelled as "dichoromethylene diphosphonate." Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,635,600 to Fanger et al. (A4 on form PTO-1449) in view of U.S. Patent No. 5,922,845 to Deo et al (A on form PTO-892) as applied to claim 13 above, and further in view of Naito et al (J. Leuk. Biol. [1996] 60(3):337-344; U on form PTO-892, newly cited).

The '600 and '845 patents have been discussed supra.

The combined references do not teach liposomes comprising dichloromethylene diphosphonate as the toxin for killing macrophages.

Naito teaches that liposome-encapsulated dichloromethylene diphosphonate is used in the art to selectively deplete macrophages (page 337, column 1 in particular). Naito further teaches that the apoptotic agent dichloromethylene diphosphonate in solution is not toxic to cells in solution and apparently does not easily pass through a cell membrane (page 341, second column in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use liposome-encapsulated dichloromethylene diphosphonate as a toxin for the killing of monocytic cells attached to the antibody of the '600 patent. One would have been motivated to combine the teachings, with a reasonable expectation of success, by the teachings of the '600 patent that cell toxins attached to the antibody could be contained in a liposome and by the teaching of Naito that dichloromethylene diphosphonate must be ingested by the target cell because the agent cannot pas through the cell membrane on its own, therefore making the agent harmless to cells not specifically targeted by the antibody, even after the release of the agent after the death of the targeted cells.

8. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,635,600 to Fanger et al. (A4 on form PTO-1449) in view of U.S. Patent No. 5,922,845 to Deo et al (A on form PTO-892) as applied to claims 9 and 10 above, and further in view of U.S. Patent No. 6,500,931 to Tempest et al. (filed May 4, 1995; B on form PTO-892).

The '600 and '845 patents have been discussed supra.

The combined references do not teach the humanized H22 antibody produced by ATCC cell line CRL-11177.

The '931 patent teaches H22 as a product of ATCC cell line CRL-11177 (column 3, in particular). RV

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to substitute the humanized H22 antibody for the fully murine version for use in a human subject. One would have been motivated to make the substitution with a reasonable expectation of success by the teachings of the '931 patent regarding the comparable binding properties of H22 to mAb 22 (Table 1 in particular) and by the teachings of the '931 patent that humanization of the antibody avoids the generation of a HAMA immune response (columns 1-2 in particular).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

F. Pierre VanderVegt, Ph.D. RV
Patent Examiner
March 30, 2007

David A Saunders
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